

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Previously Presented) A procytotoxin comprising a peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the  $\epsilon$ -amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the  $\epsilon$ -amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation.
2. (Previously Presented) The procytotoxin of claim 1, wherein the cytotoxic peptide is a pore-forming cytolytic peptide.
3. (Currently Amended) The procytotoxin of claim 2, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokyotorphin, neokyotorphin fragment 1, neokyotorphin fragment 2, neokyotorphin fragment 3, neokyotorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, streptolysin, ~~analog~~~~s thereof~~, and derivatives thereof **analogs of the pore-forming cytolytic peptide, and derivatives of the pore-forming cytolytic peptide.**

4. (Original) The procytotoxin of claim 3, wherein the cytolytic peptide is selected from the group consisting of amoebapores, amoebapore analogs and amoebapore derivatives.

5. (Currently Amended) The procytotoxin of claim 4, having the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R) (**SEQ ID NO: 1**), wherein at least one (R) is independently selected from the group consisting of [ε-γ]-Glu, [ε-γ]-Glu-[α-γ]-(Glu)<sub>1-3</sub>, [ε-α]-(Phe)<sub>1-3</sub>, [ε-α]-(Tyr)<sub>1-3</sub>, [ε-α]-(Trp)<sub>1-3</sub>, [ε-α]-(Lys)<sub>1-3</sub> and [ε-α]-(Arg)<sub>1-3</sub>, wherein [ε-γ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, [α-γ] represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, [ε-α] represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

6. (Original) The procytotoxin of claim 3, wherein the cytolytic peptide is a melittin, a melittin analog or a melittin derivative.

7. (Currently Amended) The procytotoxin of claim 6, ~~having~~ **consisting essentially of** the following structure: Gly- Ile-Gly-Ala-Val-Leu-Lys(R)-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys(R)-Arg-Lys(R)-Arg-Gln-Gln (**SEQ ID NO: 2**), wherein **at least one (R) is** ~~R is~~ independently selected from the group consisting of ~~the unmodified ε-amino group of the adjacent lysine residue,~~ [ε-γ]-Glu, [ε-γ]-Glu-[α-γ]-(Glu)<sub>1-3</sub>, [ε-α]-(Phe)<sub>1-3</sub>, [ε-α]-(Tyr)<sub>1-3</sub>, [ε-α]-(Trp)<sub>1-3</sub>, [ε-α]-(Lys)<sub>1-3</sub> and [ε-α]-(Arg)<sub>1-3</sub>, wherein [ε-γ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, [α-γ] represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, [ε-α]

represents a peptide bond between the epsilon amino group of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

8. (Currently Amended) A procytotoxin comprising a peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the  $\epsilon$ -amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the  $\epsilon$ -amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation, and wherein said procytotoxin has a structure selected from the group consisting of: ~~The procytotoxin of claim 1 having a structure selected from the group consisting of:~~ ~~N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Ile-Gln-Leu-Ile-Glu-Asp-Lys([ $\epsilon$ - $\gamma$ ]-Glu-[ $\alpha$ - $\gamma$ ]-Glu)-COOH~~ N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys([ $\epsilon$ - $\gamma$ ]-Glu-[ $\alpha$ - $\gamma$ ]-Glu)-CONH<sub>2</sub> (SEQ ID NO: 8) and NH<sub>2</sub>-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys([ $\epsilon$ - $\gamma$ ]-Glu-[ $\alpha$ - $\gamma$ ]-Glu)-Arg-Lys([ $\epsilon$ - $\gamma$ ]-Glu-[ $\alpha$ - $\gamma$ ]-Glu)-Arg-Gln-Gln-COOH (SEQ ID NO: 12).

9. (Original) A pharmaceutical composition, comprising the procytotoxin of claim 1, and a pharmaceutically acceptable excipient.

10. (Original) A method for selectively destroying a target cell, comprising contacting the target cell with a procytotoxin, which comprises a cytotoxic peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the  $\epsilon$ -amino group of said lysine residue.

11. (Original) The method of claim 10, wherein the cell is a cancer cell.

12. (Original) The method of claim 11, wherein said cancer cell is selected from the group consisting of prostate, ovarian, lung and skin cells.

13. (Original) The method of claim 11, wherein the cytotoxic peptide is a pore-forming cytolytic peptide.

14. (Original) The method of claim 13, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokyotorphin, neokyotorphin fragment 1, neokyotorphin fragment 2, neokyotorphin fragment 3, neokyotorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, streptolysin, and analogs and derivative thereof.

15. (Original) The method of claim 14, wherein the cytolytic peptide is selected from the group consisting of amoebapores, amoebopore analogs and amoebopore derivatives.

16. (Currently Amended) The method of claim 14, wherein the procytotoxin has the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R) (**SEQ ID NO: 1**), wherein **at least one (R) is R** is independently selected from the group consisting of ~~the unmodified  $\epsilon$ -amino group of the adjacent lysine residue,~~ [ $\epsilon$ - $\gamma$ ]-Glu, [ $\epsilon$ - $\gamma$ ]-Glu- $[\alpha$ - $\gamma$ ]- $(\text{Glu})_{1-3}$ , [ $\epsilon$ - $\alpha$ ]- $(\text{Phe})_{1-3}$ , [ $\epsilon$ - $\alpha$ ]- $(\text{Tyr})_{1-3}$ , [ $\epsilon$ - $\alpha$ ]- $(\text{Trp})_{1-3}$ , [ $\epsilon$ - $\alpha$ ]- $(\text{Lys})_{1-3}$  and [ $\epsilon$ - $\alpha$ ]- $(\text{Arg})_{1-3}$ , wherein [ $\epsilon$ - $\gamma$ ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, [ $\alpha$ - $\gamma$ ] represents a peptide bond between the alpha amino group of the first

glutamate and the gamma carboxyl group of the second glutamate,  $[\epsilon-\alpha]$  represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

17. (Original) The method of claim 14, wherein the cytolytic peptide is a melittin, a melittin analog or a melittin derivative.

18. (Currently Amended) The method of claim 17, wherein the procytotoxin ~~has~~ **consisting essentially of** the following structure: Gly-Ile-Gly-Ala-Val-Leu-Lys(R)-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys(R)-Arg-Lys(R)-Arg-Gln-Gln (**SEQ ID NO: 2**), wherein **at least one (R) is** R-is-independently selected from the group consisting of ~~the unmodified  $\epsilon$ -amino group of the adjacent lysine residue,~~  $[\epsilon-\gamma]$ -Glu,  $[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -(Glu)<sub>1-3</sub>,  $[\epsilon-\alpha]$ -(Phe)<sub>1-3</sub>,  $[\epsilon-\alpha]$ -(Tyr)<sub>1-3</sub>,  $[\epsilon-\alpha]$ -(Trp)<sub>1-3</sub>,  $[\epsilon-\alpha]$ -(Lys)<sub>1-3</sub> and  $[\epsilon-\alpha]$ -(Arg)<sub>1-3</sub>, wherein  $[\epsilon-\gamma]$  represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate,  $[\alpha-\gamma]$  represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate,  $[\epsilon-\alpha]$  represents a peptide bond between the epsilon amino group of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

19. (Currently Amended) **A method for selectively destroying a target cell, comprising contacting the target cell with a procytotoxin, which comprises a cytotoxic peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the  $\epsilon$ -amino group of said lysine residue, wherein the cell is a cancer cell and the procytotoxin has the structure** ~~The method of claim 17 wherein the procytotoxin has a structure selected from the group consisting of: N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-~~

~~Asp-Lys-Ile-Gln-Leu-Ile-Glu-Asp-Lys([ε-γ]-Glu-[α-γ]-Glu)-COOH and~~ NH<sub>2</sub>-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys([ε-γ]-Glu-[α-γ]-Glu)-Arg-Lys([ε-γ]-Glu-[α-γ]-Glu)-Arg-Gln-Gln-COOH **(SEQ ID NO: 12)**.

20. (Previously Presented) The procytotoxin of claim 2, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokyotorphin, neokyotorphin fragment 1, neokyotorphin fragment 2, neokyotorphin fragment 3, neokyotorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, and streptolysin.

21. (Previously Presented) The procytotoxin of claim 20, wherein the cytolytic peptide is an amoebapore.

22. (Currently Amended) The procytotoxin of claim 21, having the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R) **(SEQ ID NO. 1)**, wherein **at least one (R) is R** is independently selected from the group consisting of [ε-γ]-Glu, [ε-γ]-Glu-[α-γ]-(Glu)<sub>1-3</sub>, [ε-α]-(Phe)<sub>1-3</sub>, [ε-α]-(Tyr)<sub>1-3</sub>, [ε-α]-(Trp)<sub>1-3</sub>, [ε-α]-(Lys)<sub>1-3</sub> and [ε-α]-(Arg)<sub>1-3</sub>, wherein:

[ε-γ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate,

[α-γ] represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate,

[ $\epsilon$ - $\alpha$ ] represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid, and

the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

23. (Previously Presented) The procytotoxin of claim 22, wherein R is independently selected from the group consisting of [ $\epsilon$ - $\gamma$ ]-Glu and [ $\epsilon$ - $\gamma$ ]-Glu-[ $\alpha$ - $\gamma$ ]-Glu)<sub>1-3</sub>, wherein:

[ $\epsilon$ - $\gamma$ ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate,

[ $\alpha$ - $\gamma$ ] represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, and

the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

24. (New) A method for selectively destroying a target cell, comprising contacting the target cell with a procytotoxin, which comprises a cytotoxic peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the  $\epsilon$ -amino group of said lysine residue, wherein the cell is a cancer cell and the procytotoxin has the structure N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys([ $\epsilon$ - $\gamma$ ]-Glu-[ $\alpha$ - $\gamma$ ]-Glu)-CONH<sub>2</sub> (SEQ ID NO. 8).

25. (New) A procytotoxin comprising a peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the  $\epsilon$ -amino group of said lysine residue,

(i) wherein said peptide without the modification is a cytolytic peptide,

(ii) wherein said at least one amino acid bound via the  $\epsilon$ -amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation, and

(iii) wherein said cytolytic peptide need not be internalized to cause target-specific cell death.

26. (New) The procytotoxin of claim 25, wherein the cytolytic peptide is selected from the group consisting of amoebapore and melittin.